Comparison of Respiratory Rate Detection by Seven Sensor Signals in Clinically Challenging Conditions

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Abstract:

Introduction: The underlying problem for two of the three most common patterns of unexpected hospital deaths (PUHD) is hypoventilation[1]. Concern over this opioid-induced respiratory depression has led many experts and consensus guidelines to recommend that all patients receiving opioids be monitored for respiratory rate. Currently, no clinically accepted "gold-standard" monitoring device exists for non-intubated, spontaneously breathing patients. We studied seven distinct respiratory sensors to compare their effectiveness in respiratory monitoring. Methods: With IRB approval, data were collected from 26 volunteers who were administered target controlled infusions of remifentanil and propofol in order to induce low respiratory rates. Data were collected from a suite of sensors which were analyzed using a single, custom breath detection algorithm. Breath rates derived from a capnometer, accelerometer, oro-nasal thermistor, nasal pressure transducer, microphone, photoplethysmogram, and impedance respiratory sensor were compared against breath rates derived from the reference standard of respiratory inductance plethysmography bands at both low and normal respiratory rate ranges. Results: Capnometry and acceleromtry reported respiratory rates closest to those reported by the respiratory inductance plethysmography bands. Conclusion: Detecting respiratory rate in the post-operative environment is a clinically challenging problem which likely requires further study.

INTRODUCTION & BACKGROUND

The underlying problem for two of the three most common patterns of unexpected hospital deaths (PUHD) is hypoventilation[1]. Type II PUHD (CO_2 narcosis) involves a reduction in respiratory rate and/or tidal volume, and if supplemental oxygen is being provided, a pulse oximeter will not detect the problem until the hypercarbia is significantly advanced and the patient is near respiratory arrest. Type III PUHD is induced by obstructive sleep apnea in the presence of arousal failure, and is recognized as a repetitive sequence of cyclic apneas and self-arousals which precede the final apnea. A pulse oximeter alarms with each apneic period and will likely be interpreted as generating many false positive alarms.[1] The risk of opioid-induced respiratory depression in postoperative patients is greatest in the first 24 hours after initiation of opioids[2], and opioids are the most commonly used drug for treating pain in the postoperative period.[3]

These problems would be especially troublesome during long-range, manned space missions where monitoring personnel are limited due to either sedation of crew members or an injury rendering the crew short-handed.

Respiratory depression is caused by drug-induced inhibition of the breathing control center of the brain stem. Partial to full airway obstruction is an anatomic problem involving the soft palate, tongue base, and/or epiglottis, caused by drug-induced

decreases in airway patency and muscle tone. Sedatives and opioids depress the response to elevated CO_2 (reduced drive to breathe), worsen arousal, cause airway obstruction, and change sleep patterns[4-8]

In the postoperative period, most adverse respiratory events occur during the first 24 hours of opioid administration.[2] During this period, pulse oximeter monitoring, supplemental oxygen, incentive spirometry, and intermittent nursing observation are the primary interventions used to fend off adverse respiratory events. For inpatient monitoring, pulse oximetry is often inadequate. On a busy hospital floor, it is difficult to respond to multiple remote advisory pulse oximetry alarms. Pulse oximeter alarms are ignored because they have a high false-positive alarm rate due to movement artifact and displacement.[9,10] Pulse oximetry primarily monitors oxygenation instead of ventilation; the SpO_2 signal is a delayed indicator for apnea or hypopnea, particularly when supplemental oxygen is given. By the time the pulse oximeter alarms, an apneic patient is already in danger of hypoxia, brain injury and death.

Despite exhaustive studying of respiratory monitoring technologies, no sensor has emerged as a clinically accepted gold-standard for non-intubated, spontaneously breathing patients[11]. Monitors which are currently used elsewhere in the healthcare environment may not be suited to this situation. Capnometry, often used during intubations, relies on an adequate gas sample from the airway which may be difficult to obtain in the non-intubated environment. Pulse oximetry is notoriously delayed in detecting apnea, especially when patients are receiving supplemental oxygen. In addition, neither of these monitoring modalities distinguish between central apnea and obstructive apnea, which may influence clinical decision making.

We suggest that there is an urgent need for a low cost, reliable respiratory depression monitoring technique that can be integrated with the signals from the pulse oximeter to give additional physiologic information about a patient's sufficiency of both ventilation and oxygenation in the non-intubated setting.

Currently, we are exploring the value of integrating the information from a set of low-cost physiologic monitors to detect respiratory rate. Specifically, we studied a capnometer, accelerometer, nasal pressure transducer, thermistor, peri-tracheal microphone, photoplethysmogram, chest impedance, and respiratory inductance plethysmography.

We tested each sensor under identical conditions in order to reduce as many variables as possible in the comparison. Specifically, each sensor recorded data from the same subjects, and during the same time period. An identical, threshold-based breath detection algorithm was then implemented on each signal in order to detect breathing. The goal was to establish the comparative strengths and weaknesses of each sensor in different respiratory rate ranges.

METHODS

Informed written consent was obtained from 26 volunteers (13 male, 13 female). Eligible volunteers had an ASA physical status of I or II, age 18 to 55 years, body mass index between 18 and 30 kg/m2, negative drug screen, and uncomplicated airway anatomy. Volunteers were not eligible if they had a history of significant alcohol or drug abuse, a positive drug-screening test, allergy to opioids or propofol, obstructive sleep apnea, any prescription medication intake other than

oral contraceptives in the 48 hours preceding the study, or medical illnesses that are known to alter the pharmacokinetics or pharmacodynamics of opioids or intravenous anesthetics.

Volunteer subjects were instrumented with a three lead electrocardiogram that detects respiratory rate using chest impedance (Datex Ohmeda, GE Healthcare, Helsinki, Finland), a photo-plethysmography (PPG) sensor (SET, Masimo Corporation, Irvine, CA), an abdominal accelerometer sensor (ADXL345, Analog Devices, Norwood, MA), respiratory inductance plethysmography (RIP) chest bands (Q-RIP, Braebon Medical Corporation, Kanata, ON, Canada), a capnometer nasal cannula (LoFlo, Philips Medical, Wallingford CT), a nasal airway pressure sensor (1 INCH-D-4V, All Sensors, Morgan Hill, CA), a nasal/oral thermistor (Disposable Adult Airflow Sensor, Braebon Medical Corporation, Kanata, ON, Canada), and a peri-tracheal microphone (Audio-Technica ATR3350iS. Machida, Tokio, Japan) positioned within a metal pre-cordial stethoscope cup (Wenger #00-390-c, AINcA, San Marcos, CA) placed just below the larynx and above the suprasternal notch. Data waveforms were digitized at 100 Hz with the exception of the acoustic waveform which was digitized at 44.1 kHz.

A 20 gauge venous catheter was placed in an antecubital vein under local anesthesia (0.2 mL of 0.5% lidocaine) for the purpose of hydration and drug administration. The IV site was similar in all subjects. A maintenance infusion of 0.9% sodium chloride was administered at 1 ml/kg/hour throughout the study. Continuous infusions of Remifentanil and Propofol was infused into this peripheral IV.

Our team previously characterized various effects of sedatives combined with opioids using drug interaction models. Specifically, we characterized the interaction of Propofol and Remifentanil on metrics of airway obstruction and intolerable ventilatory depression in volunteers.[8] Each subject received Propofol and Remifentanil. Similar to previously collected data from our volunteer laboratory (Kern et al, 2004), each drug was administered using a computer controlled (Stanpump[14]) continuous infusion pump (Pump 22; Harvard Apparatus, Limited, Holliston, MA) to achieve selected target effect site concentrations. The effect site concentration refers to the drug concentration at the pharmacologic site of action. Pharmacokinetic parameters published by Minto *et al.*[15] and Schnider et al.[16] was used for Remifentanil and Propofol respectively.

We administered Propofol and Remifentanil pairs in a dose escalation scheme with small steps in order to creep up to the desired target effects of respiratory depression, airway obstruction and both effects while avoiding overshoot. To accomplish this, the Propofol was dosed in a range of 0.75 - 4 mcg/mL in dose escalation steps of approximately 0.5 mcg/mL. Remifentanil was dosed in a range of 0.75 to 4.0 ng/mL in escalation steps of approximately 0.25-0.5 ng/mL.

Data were isolated from periods during which the patient was unperturbed, not talking, and breathing normally (no obstruction present). Samples of all acquired waveforms and the filteres used to process them are shown in Figure 1.

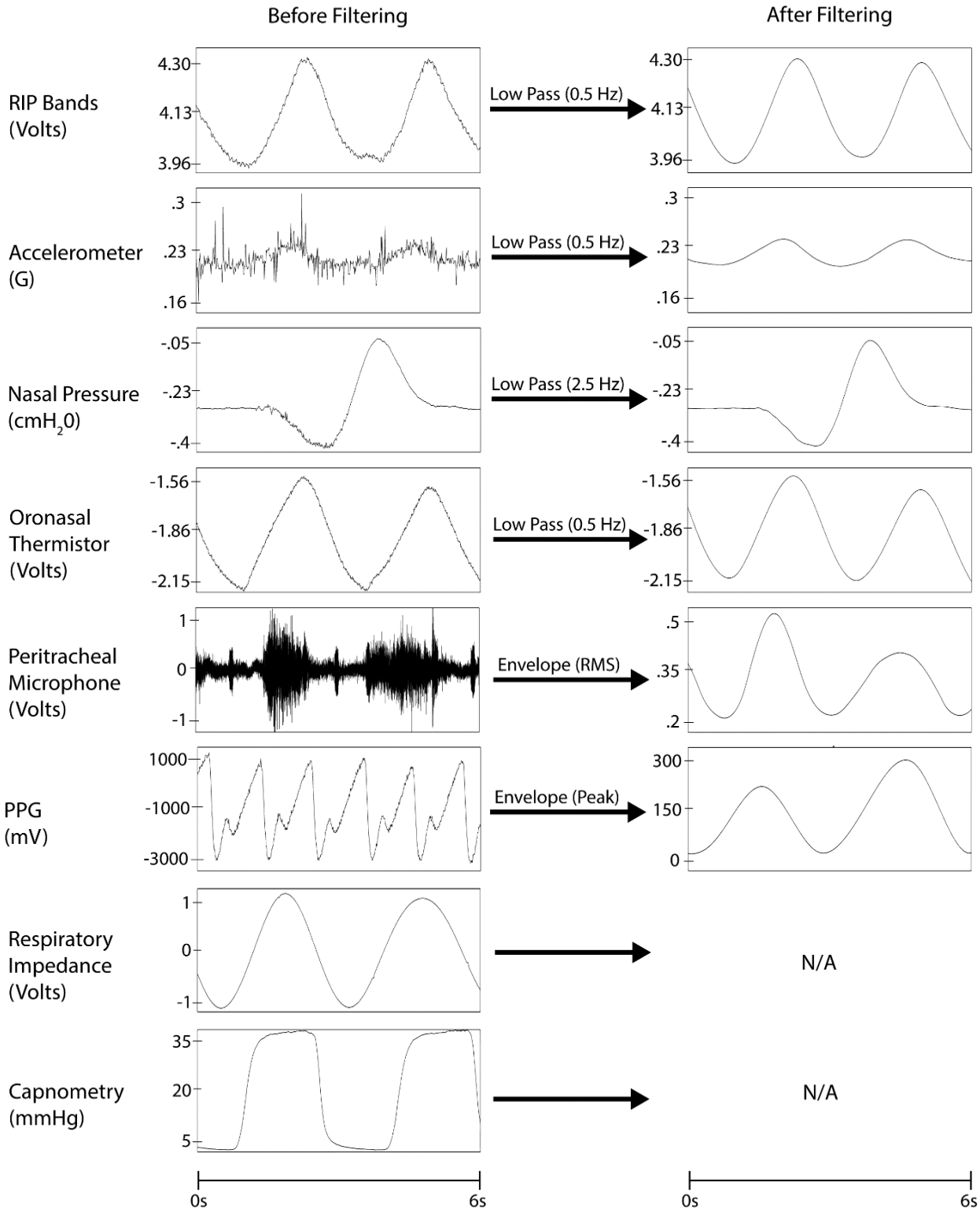

Figure 1: Raw signal waveforms before and after filtering. Filters used are indicated on the transitional arrows. PPG indicates photoplethysmography.

A custom algorithm which detects peak prominence in each signal and compares it to predefined thresholds was used to detect breathing in each signal. Respiratory rate during each acquired minute of data was calculated for each sensor and compared to the reference standard of respiratory inductance plethysmography.

A Bland-Altman style analysis was performed on two sets of data. In one set, all respiratory rate ranges were included. In the second set, only data where the reference respiratory rate was 10 or fewer breaths per minute was used. In these analyses, bias is calculated as the mean difference in the respiratory rates reported by the reference and comparison sensor signals (reference minus comparison). Standard deviation is the square root of the statistical variance that assumes a normal distribution. A 95% confidence interval is calculated as bias ± standard deviation. A sample Bland-Altman style plot is presented in figure 2.

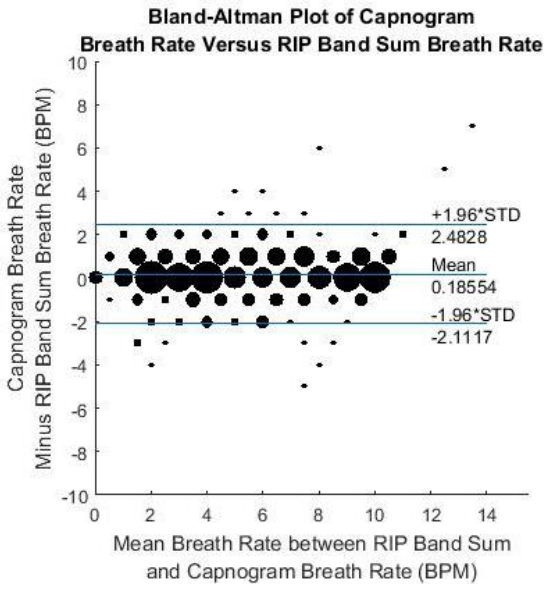

Figure 2: Blant-Altman style plot comparing capnometry against Respiratory Inductance Plethysmography at respiratory rate of 10 or fewer breaths per minute.

RESULTS

A total of 877 minutes of data fit the criteria described in the methods. The results of the Bland-Altman analysis which includes all respiratory rates is presented in Table 1. The accelerometer, nasal pressure, thermistor, and capnometer all exhibited low bias (<.4 BPM). Impedance, photoplethysmogram, and microphone all exhibited relatively high bias (1.4-2 BPM). The signals with the lowest standard deviation were the accelerometer and the capnometer. The highest standard deviations were exhibited by the respiratory impedance, photoplethysmogram, and microphone.

A total 407 minutes were available where the reference signal reported a respiratory rate of 10 or fewer breaths per minute. The results of the Bland-Altman analysis on this data set is presented in Table 2. All signals exhibited low bias (-.6 BPM). The signals with the lowest standard deviation were the accelerometer and capnometer.

CONCLUSION

A low cost, accurate, and minimally sized respiratory monitor would be useful during space travel when personnel are limited following an injury/emergency procedure or if astronauts were to be sedated during extended voyages.

Overall, obtaining accurate respiratory rates in non-intubated, spontaneously breathing volunteers is challenging. We were able to obtain reasonably reliable respiratory rates from two signals—an accelerometer and capnometer. These signals generally exhibited the lowest signal-to-noise ratio and lowest amount of signal drop-out. The impedance primarily struggled with a low signal-to-noise ratio that stemmed from cardiogenic motion. The thermistor primarily

Table 1: Bland-Altman summary statistics for all sensors and all respiratory rate ranges. PPG indicates photoplethysmography.

	Accelerometer	Nasal Pressure	Thermistor	Impedance	Capnometer	PPG	Microphone
Bias (BPM)	-0.30	-0.40	-0.20	-1.40	0.00	-2.00	-1.70
Std (BPM)	1.89	2.76	2.34	4.95	1.25	4.87	4.52
Upper 95% Confidence Interval (BPM)	3.40	5.00	4.40	8.30	2.50	7.50	7.20
Lower 95% Confidence Interval (BPM)	-4.00	-5.80	-4.80	-11.10	-2.50	-11.50	-10.60

Table 2: Bland-Altman summary statistics for all sensors and low respiratory rate ranges (10 or fewer breaths per minute as detected by the reference signal). PPG indicates photoplethysmography.

	Accelerometer	Nasal Pressure	Thermistor	Impedance	Capnometer	PPG	Microphone
Bias (BPM)	0.10	0.00	0.50	0.60	0.20	0.40	0.20
Std (BPM)	1.08	2.49	2.07	3.92	1.17	3.03	2.15
Upper 95% Confidence Interval (BPM)	2.20	4.90	4.60	8.30	2.50	6.30	4.40
Lower 95% Confidence Interval (BPM)	-2.00	-4.90	-3.60	-7.10	-2.10	-5.50	-4.00

struggled with high sensitivity to external airflows. In the case of the microphone and the photoplethysmogram, the filtering method was a concern. Both signals have much higher underlying frequencies (sound and heart rate) that had to be filtered out using an envelope filtering technique. This method may have been imperfect for assessing respiratory rate in these signals.

There were many other limitations to consider when analyzing these results. All data was collected from healthy volunteers who instructed to lay quietly. This may not reflect the clinical condition. Additionally, subjects were receiving 2 L/min of oxygen through a nasal cannula which may have had an effect on the nasal pressure, thermistor, and capnometer signals. Additionally, the algorithm may not be as suited to some signal waveforms as others (as noted in the case of the photoplethysmogram and microphone).

The comparison in signal performance between high and low respiratory rates may help influence decision making when choosing a sensor to monitor patients who are at risk of developing respiratory complications. All signals improved when monitoring for low respiratory rates, however the accelerometer had the highest relative improvement, indicating it may be especially suited to detecting these clinical conditions.

We intend to continue this analysis and analyze how each signal performs in detecting specific clinical pathologies. Additionally we will study whether accuracy can be improved through sensor fusion techniques.

ACKNOWLEDGEMENTS

I would like to thank the Rocky Mountain Space Grant Consortium for providing funding in order to pursue this research.

I would also like to thank those individuals who are currently assisting not only in data collection and planning but also in general advice during this study. Those individuals are Soeren Hoehne, Kelly Smith, Ken Johnson, and Julia White.

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